# NEW YORK PATHOLOGICAL SOCIETY

## ABSTRACT OF PAPER AND DISCUSSION

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## *Involvement of the Nervous System by Bronchogenic Carcinoma*

WILLIAM HENRY MCMENEMEY

Institute of Neurology of the University of London,
Maida Vale Hospital for Nervous Diseases, London, England

Dr. McMenemey discussed the incidence of bronchial carcinoma in different types of hospitals, comparing published figures with his own. Comparison was often difficult because melanoma was sometimes included and sometimes not. In his own series, in which melanocarcinoma had been included, a bronchial origin was established in 52.5 per cent of cases. In a neurological hospital the primary tumor is usually silent and the search for it both clinically and at necropsy may prove difficult. Unless the histologic diagnosis has been established beyond doubt in a case of cerebral tumor, the lungs, after routine examination at necropsy, should be preserved for more detailed studies in case the diagnosis proves to be one of metastatic carcinoma of the brain. The association of metastases in the adrenals and brain was suggestive of a primary site in the lung, especially in a male. The speaker compared present-day statistics with earlier ones, more especially those of Krasting (1906)[1], and concluded that there had been a definite increase in the disease.

The symptomatology of carcinomatous involvement of the nervous system, he said, was protean, and the disease might present in many unusual ways. He gave several examples, including one which first showed as a cerebellar hemorrhage and another as an acute cauda equina syndrome. The clinical course of a bronchial metastasis in the brain might at times be so slow as to throw doubt on the diagnosis. Dr. McMenemey drew attention to the frequency with which the meninges were involved, sometimes without any obvious discrete secondary tumor being present in the brain. He and his colleague, Dr. J. N. Cumings, in a large series of cases of histologically confirmed tumor of the brain, had noticed that the cerebrospinal fluid cell count was raised above 5 in 20.4 per cent of cases of intracranial carcinoma, over 10 in 15.3 per cent, and over 20 in 8.5 per cent. Very often tumor cells could be identified. On occasion they had been found when the total cell count was within the normal range. If, therefore, a diagnosis of carcinomatosis of the brain were under consideration, a search of the deposit for the presence of carcinoma cells was always worth while. The significance of a falling glucose content in the cerebrospinal fluid was also discussed.

Dr. McMenemey described the findings in three cases of cerebellar degeneration in association with carcinoma, a rare but important combination. However, its incidence was sometimes underestimated because in a very sick person cerebellar symptoms and signs might not be easily apparent. In general the disease seemed to be associated with small primary tumors, and metastases in the brain and elsewhere were more often absent than present. He described also examples of

carcinomatous neuropathy, pointing out that in this disease, as well as in cerebellar degeneration, the degeneration did not proceed *pari passu* with the growth of the primary tumor. The presence of either cerebellar degeneration or a carcinomatous neuropathy in a previously well patient should encourage a hunt for a primary tumor. The speaker then discussed the possibility of there being a specific form of cortical degeneration associated with the presence of carcinoma, and instanced the work of Brierley and Charatan (1956)[2]. He discussed the significance in cerebellar degeneration of the lymphocytic infiltration sometimes found; also a first zone Lange curve. Finally, he compared the incidence of bronchial carcinoma in Britain with that in the United States, concluding that it was not smoking alone, nor atmospheric pollution alone which accounted for the prevalence of the disease, but a summation of insults to the bronchial mucosa associated with civilization. To discourage smoking was the one quick way of reducing the insult, and at the same time, of diminishing the alarmingly increased incidence of the disease.

## *DISCUSSION*

JOHN G. KIDD: A few years ago I lent Dr. Willis' book, *The Spread of Tumors,* to one of my students. When I asked him what he got out of it, he said that he could summarize the whole book in a single sentence: "A tumor arises anywhere in the body, and spreads anywhere in the body." What we have seen this evening is that bronchogenic carcinomas have the capacity to spread not only to the brain, but to other parts of the nervous system under circumstances that are little short of bizarre. Dr. Zimmerman, a distinguished member of our Society, is in the audience. Since he has had wide experience in lesions of the central nervous system, I wonder whether he would be good enough to give us his evaluation of his own experience in comparison with this of Dr. McMenemey.

HARRY M. ZIMMERMAN: All of us know Dr. McMenemey as a neuropathologist and as the superb architect of the International Neuropathological Congress in London, which some of us in this audience will never forget. This is a marvellous opportunity for those who are general pathologists to compare notes with you, Dr. McMenemey, since you are both a general pathologist and a neuropathologist. I have a few questions to ask you. One is, how often have you seen carcinoma in cases of multiple sclerosis? This is a question I have been asked innumerable times by such people as Hans Reese in this country and others interested in multiple sclerosis, following a statement by Schaltenbrand of Germany to the effect that the two diseases are incompatible. I was therefore astonished to find in our Multiple Sclerosis Registry, which we carry on at our Hospital, that 8 to 10 per cent of cases of multiple sclerosis have carcinoma of one organ or another, not necessarily of the lung.

The remark that Dr. Kidd made that tumors may arise anywhere and go anywhere (and the lung is one of these organs) brings to mind the fact that in our experience, and in yours, carcinoma of the lung is by far the most frequent primary site of central nervous system metastases. In some 1400 cases of pulmonary carcinoma we had, I believe, several hundred which went to the brain, which is by all odds the most frequent site of metastasis from any primary carcinoma anywhere in the body. Next in frequency in our hospital is breast carcinoma, but unlike the pulmonary carcinomas, the breast tumors go to the intracranial dura and to the spinal dura much more frequently than they do to the parenchyma of the central nervous system.

There are a few other things that Dr. Kidd's remark brought to my attention. We have seen a number of cases of carcinoma of the urinary bladder with metastases to the brain, and almost invariably when apparently primary metastases occur in these odd sites there is an intermediate station in the lung. We have found repeatedly that a bizarre type of tumor, one that rarely goes to the brain, when it does so, almost always goes by way of an intermediate station in the lung.

You have not mentioned, Dr. McMenemey, malignant lymphomas of the nervous sys-

tem, and I am not referring to those associated necessarily with malignant lymphoma in the bone marrow or lymph nodes. I have now some 16 cases of primary lymphoma in the central nervous system, among them reticulum cell sarcomas, lymphosarcomas, Hodgkin's disease, and so forth. Do you see them in your collection?

LIONEL S. AUSTER: Inasmuch as my avocation is that of a pathologist, and my true vocation is that of a surgeon interested in tumor pathology, perhaps you will bear with me for a moment, because Dr. McMenemey's magnificent array of material, in spite of the fact that his title did not limit involvement, nevertheless was almost exclusively shown in the brain. In at least one instance he was able to show some posterior nerve root involvement as evidence of peripheral neuropathy, and I should like not only to call attention to this group, but to request help and information to explain the reason for a most important symptomatic aspect of morbidity in pulmonary carcinoma: the neuralgia or neuropathy producing pain incidental to lesions found more particularly in the upper lobe, the so-called sulcus tumors. These notoriously produce bizarre, seemingly unrelated symptoms even before there is demonstrable evidence of true pulmonary parenchymatous involvement. I have seen in my own scant personal experience at least half a dozen cases in which the paresis of one vocal cord plus a peculiar irritative cough is the only early symptom, without anything else that might help one to suspect the presence of an upper lobe tumor. Another sign is the Horner syndrome. Moreover, there is a type of upper lobe tumor which very rapidly involves the upper and posterior mediastinum, with erosion of the anterior surface of the vertebral bodies, affecting, strangely enough, not the anterior roots, but the posterior spinal nerve roots, with severe pain referable to C-6 and 7 and T-1, 2 and 3, and radiation to the neck, the shoulder, and axilla. The cause is eventually, after a long time, demonstrable as a lesion arising from the lung and in the upper posterior mediastinum. Only after the most detailed roentgen studies in the oblique position will such erosion and bone involvement sometimes show. For relief of pain these patients receive high dosage radiation therapy, and now, with the advent of cobalt therapy, relief is better than previously. But they are never completely relieved, despite occasional shrinkage of the tumor. As Dr. Sala and I showed in a study of the causes of death in cancer of the cervix[3], and a similar situation is seen in cancer of the prostate, after extensive radiation therapy without any evidence of residual tumor in or about the primary sites, there is not only a contraction as a result of fibrosis, but also persistence of carcinoma in the periureteral and perineural lymphatics in the pelvis and lower abdomen, which accounts for the pain. I wonder whether anyone has seen, or has had the opportunity to dissect, posterior nerve roots in lung cancer cases to see why it is that these patients have persistent pain which is subjectively far worse than that caused by the essential primary lesion.

I believe perineural lymphatic involvement is the answer.

In connection with the reported excess of pulmonary carcinoma prevalent in the United Kingdom compared with that in the United States, I am also tempted to state that perhaps one of the reasons is that the British make those extremely irritating and highly carcinogenic types of cigarettes that are made from pure Virginia tobacco.

WILLIAM H. McMENEMEY: In reply to Dr. Zimmerman's question concerning the coexistence of carcinoma with multiple sclerosis, I can only recall one case, many years ago. I think that most cases of multiple sclerosis die before they get into the carcinoma age group. That may be one reason, but we do not get many bodies for postmortem showing the pathology of multiple sclerosis. More usually we receive only the brain and cord, with the information that a complete necropsy has been carried out and nothing else found. I am much interested to hear your experience concerning this association. I agree absolutely about carcinoma of the breast and its tendency to involve the dura. It is very striking in many of the ones we have had. I have seen only one instance of carcinoma of the

bladder metastasizing to the brain, and I cannot recall whether there was a lesion of the lung, but I would expect that there was.

We have had some cases of malignant lymphoma, but they have mostly been lesions of the cord; we have had a few instances, however, of reticulum cell sarcoma involving the brain.

In reply to Dr. Auster, the so-called Pancoast syndrome, I think, is the one you mean. I have not had any for some years—not since I have been working in a neurological hospital, but I do remember having seen them previously at another hospital. I believe they had pain, but the roots were not studied microscopically. I am grateful for your remarks and agree that these cases would repay more detailed study.

MORRIS F. WIENER: Is it feasible to routinely examine the spinal fluid for malignant cells in all cases of bronchogenic carcinoma, especially where radical surgery is contemplated? This question is suggested by the purported high incidence of central nervous system involvement in carcinoma of the lung.

WILLIAM H. McMENEMEY: Yes, if there are the slightest clinical grounds for believing that the central nervous system is already involved.

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